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TECH CENTER 1600/2900

SEQUENCE LISTING

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TECH CENTER 1600/2900

<110> BOYLE, WILLIAM LACEY, DAVID CALZONE, FRANK CHANG, MING\SHI SENALDI, GIORGIO

<120> COMBINATION THERAPY FOR CONDITIONS LEADING TO BONE LOSS

<130> A-378CIP5

<140> US 09/613,591

<141> 2000-07-10

<150> US 09/457,647

<151> 1999-12-09

<150> US 09/350,670

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<150> US 08/706,945

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Liggagg	cag agtttctttc a	81
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~223/	rea primer	
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tgcatta	cga t	71
cgcacca	egu c	/ <u>T</u>
	74	
<211>	43	
	DNA	
	Mus musculus	
~213/	Musculus	
400		
	74	
gttctcc	tca tatgaaagaa actctgcctc caaaatacct gca	43
	-	
<210>	75	
	76	
<212>	DNA	
<213>	Mus musculus	
•		
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	· -	60
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tgaacct	gat tcccta	76

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tacgcactgg atccttataa gcagcttatt tttactgatt
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tatgttaatg ag
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<210><211><212><212><213>	90 38 DNA Artificial Sequence	
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ttggaggcag agtttctttg tcgtcgtcgt cg
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      misc_feature
<223>
      Used to produce fusion protein with human OPG.
<400> 93
                                                                      26
acaaacacaa tcgatttgat actaga
<210> 94
<211> 50
<212> DNA
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      misc_feature
<223> Used to produce fusion protein with human OPG.
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                                                                      50
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      95
<211>
      50
<212> DNA
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<221>
      misc_feature
<223> Used to produce fusion protein with human OPG.
                                                                      50
catcaccatc acgaaacctt cccgccgaaa tacctgcact acgacgaaga
<210>
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<212>
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<223> Used to produce fusion protein with human OPG.
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aacctc	ccae cagetgetgt gegacaaatg ceegeegggt acceaaaca	49
<210><211><212><213>	97 26 DNA Artificial Sequence	
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                                                                     48
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<211>
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<212> DNA
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                                                                     31
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      104
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                                                                     59
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      105
<211>
      54
<212> DNA
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                                                                     54
<210>
      106
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      31
<212>
      DNA
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<400> 106
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<211> 44
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<223> PCR primer for FchOPG fusion protein.
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cagcccgggt aaaatggaaa cgtttcctcc aaaatatctt catt
                                                                     44
      108
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<211>
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	misc_feature PCR primer for FcmuOPG fusion protein.	
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<400> gaaaata	111 aaga tgcttagctg cagctgaacc aaaatc	36
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<213> Artificial Sequence
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<221> misc_feature
<223> PCR primer for huOPG-Fc fusion protein.
<400> 113
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<210>
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<221>
      misc_feature
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<400> 114
                                                                      35
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      115
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<212> DNA
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<223> Linker with XbaI and KpnI sites inserted into human sequence.
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                                                                      60
                                                                     102
aactagtcat cagctgctgt gtgataaatg tccgccgggt ac
<210>
      116
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      94
<212>
      DNA
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      Artificial Sequence
<220>
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      misc_feature
      Linker with XbaI and KpnI sites inserted into human sequence.
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                                                                      60
ttggagcaaa agtttccata tgttattcct cctt
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<212> DNA
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<221>
      misc_feature
      Linker with XbaI and SpeI sites inserted into human sequence.
<223>
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aa 6
<210> 118 <211> 62 <212> DNA <213> Artificial Sequence
<220> <221> misc_feature <223> Linker with XbaI and SpeI sites inserted into human sequence.
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tt 6
<210> 119 <211> 51 <212> PRT <213> Homo sapiens
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Tyr His Tyr Tyr Asp Gln Asn Gly Arg Met Cys Glu Glu Cys His Met 1 5 10 15
Cys Gln Pro Gly His Phe Leu Val Lys His Cys Lys Gln Pro Lys Arg 20 25 30
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Asp Trp His 50
<210> 120 <211> 2432 <212> DNA <213> Rattus rattus
<220> <221> CDS <222> (124)(1326)
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ggcagcagag aagcacctag cactggccca gcggctgccg cctgaggttt ccagaggacc 120
aca atg aac aag tgg ctg tgc tgt gca ctc ctg gtg ttc ttg gac atc 168 Met Asn Lys Trp Leu Cys Cys Ala Leu Leu Val Phe Leu Asp Ile 1 5 10 15
att gaa tgg aca acc cag gaa acc ttt cct cca aaa tac ttg cat tat Ile Glu Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr 20 25 30
gac cca gaa acc gga cgt cag ctc ttg tgt gac aaa tgt gct cct ggc Asp Pro Glu Thr Gly Arg Gln Leu Leu Cys Asp Lys Cys Ala Pro Gly 35 40 45

					aca Thr 55					312	
					aca Thr					360 -	
					tgc Cys					408	
					cga Arg					456	
					ttg Leu					504	
					acc Thr 135					552	
-	_	_	_		tca Ser	 		_		600	
					agc Ser					648	
					aat Asn					696	
					gtc Val					744	
					att Ile 215					792	
					aaa Lys					840	
					caa Gln					888	
					gac Asp					936	
					agc Ser					984	
					ctc Leu 295					1032	



					acg aga aa Thr Arg Ly 315		1080
					ttg tgg ag Leu Trp Ar		1128
					tac gca ct Tyr Ala Le		1176
				r Val Thr	cac agt ct His Ser Le 36	u Arg Lys	1224
	g Phe Leu				cga ttg ta Arg Leu Ty 380		1272
					tca gtg aa Ser Val Ly 395		1320
tgc tta ta Cys Leu 400	gttaggaa t	ggtcact	gg gctg	tttctt ca	ggatgggc ca	acactgat	1376
ggagcagatg	gctgcttct	c cggct	cttga a	atggcagtt	gattcctttc	tcatcagttg	1436
gtgggaatga	agatcctc	a gccca	acaca c	acactgggg	agtctgagtc	aggagagtga	1496
ggcaggctat	ttgataatt	g tgcaaa	agctg c	caggtgtac	acctagaaag	tcaagcaccc	1556
tgagaaagag	gatatttt	a taacci	tcaaa c	ataggccct	ttccttcctc	tccttatgga	1616
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gcaagtgctc	taccactga	g ctaaat	tctcc a	acccctgaa	ggcctctttc	tttctgcctc	1796
tgatagtcta	tgacattct	t ttttc	tacaa t	tcgtatcag	gtgcacgagc	cttatcccat	1856
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agtatgaaaa	ataatcaac	a aattti	tattc c	ttctatcaa	cattggctag	ctttgtttca	2096
gggcactaaa	agaaactac	t atatg	gagaa a	gaattgata	ttgcccccaa	cgttcaacaa	2156
cccaatagtt	tatccagct	g tcatgo	cctgg t	cagtgtct	actgactatg	cgccctctta	2216
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gtgttaaagg	cttttatta	a aaagct	tgatg c	cttctgta	aaagttacta	atatatctgt	2396
aagactatta	cagtattgo	t atttat	tatcc a	ccag			2432

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<211> 401

<212> PRT

<213> Rattus rattus

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20 25 30

Pro Glu Thr Gly Arg Gln Leu Leu Cys Asp Lys Cys Ala Pro Gly Thr 35 40 45

Tyr Leu Lys Gln His Cys Thr Val Arg Arg Lys Thr Leu Cys Val Pro 50 60

Cys Pro Asp Tyr Ser Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys 70 75 80

Val Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Thr Val Lys Gln Glu 85 90 95

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Glu Glu Gly Arg Tyr 100 105 110

Leu Glu Leu Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Leu 115 120 125

Gly Val Leu Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg 130 135 140

Cys Pro Asp Gly Phe Phe Ser Gly Glu Thr Ser Ser Lys Ala Pro Cys 145 150 155 160

Arg Lys His Thr Asn Cys Ser Ser Leu Gly Leu Leu Ile Gln Lys 165 170 175

Gly Asn Ala Thr His Asp Asn Val Cys Ser Gly Asn Arg Glu Ala Thr 180 185 190

Gln Asn Cys Glu Ile Asp Val Thr Leu Cys Glu Glu Ala Phe Phe Arg 195 200 205

Phe Ala Val Pro Thr Lys Ile Ile Pro Asn Trp Leu Ser Val Leu Val 210 215 220

Asp Ser Leu Pro Gly Thr Lys Val Asn Ala Glu Ser Val Glu Arg Ile 225 Lys Arg Arg His Ser Ser Gln Glu Gln Thr Phe Gln Leu Leu Lys Leu 245 250 Trp Lys His Gln Asn Arg Asp Gln Glu Met Val Lys Lys Ile Ile Gln Asp Ile Asp Leu Cys Glu Ser Ser Val Gln Arg His Ile Gly His Ala Asn Leu Thr Thr Glu Gln Leu Arg Ile Leu Met Glu Ser Leu Pro Gly Lys Lys Ile Ser Pro Asp Glu Ile Glu Arg Thr Arg Lys Thr Cys Lys Pro Ser Glu Gln Leu Leu Lys Leu Leu Ser Leu Trp Arg Ile Lys Asn Gly Asp Gln Asp Thr Leu Lys Gly Leu Met Tyr Ala Leu Lys His Leu 350 Lys Ala Tyr His Phe Pro Lys Thr Val Thr His Ser Leu Arg Lys Thr 360 Ile Arg Phe Leu His Ser Phe Thr Met Tyr Arg Leu Tyr Gln Lys Leu 375 Phe Leu Glu Met Ile Gly Asn Gln Val Gln Ser Val Lys Ile Ser Cys 390 Leu

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<213> Mus musculus

<220>
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<222> (91)..(1293)

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ctc Leu	ctg Leu 10	gtg Val	ctc Leu	ctg Leu	gac Asp	atc Ile 15	att Ile	gaa Glu	tgg Trp	aca Thr	acc Thr 20	cag Gln	gaa Glu	acc Thr	ctt Leu	162
														ctc Leu		210
														aca Thr 55		258
														acg Thr		306
agc Ser	tgg Trp	cac His 75	acc Thr	agt Ser	gat Asp	gag Glu	tgt Cys 80	gtg Val	tat Tyr	tgc Cys	agc Ser	cca Pro 85	gtg Val	tgc Cys	aag Lys	354
														cga Arg		402
														ttg Leu		450
cac His	cgg Arg	agc Ser	tgt Cys	ccc Pro 125	ccg Pro	ggc Gly	tcc Ser	ggc Gly	gtg Val 130	gtg Val	caa Gln	gct Ala	gga Gly	acc Thr 135	cca Pro	498
gag Glu	cga Arg	aac Asn	aca Thr 140	gtt Val	tgc Cys	aaa Lys	aaa Lys	tgt Cys 145	cca Pro	gat Asp	Gly aaa	ttc Phe	ttc Phe 150	tca Ser	ggt Gly	546
gag Glu	act Thr	tca Ser 155	tcg Ser	aaa Lys	gca Ala	ccc Pro	tgt Cys 160	ata Ile	aaa Lys	cac His	acg Thr	aac Asn 165	tgc Cys	agc Ser	aca Thr	594
														aac Asn		642
tgt Cys 185	tcc Ser	gga Gly	aac Asn	aga Arg	gaa Glu 190	gcc Ala	acg Thr	caa Gln	aag Lys	tgt Cys 195	gga Gly	ata Ile	gat Asp	gtc Val	acc Thr 200	690
ctg Leu	tgt Cys	gaa Glu	gag Glu	gcc Ala 205	ttc Phe	ttc Phe	agg Arg	ttt Phe	gct Ala 210	gtt Val	cct Pro	acc Thr	aag Lys	att Ile 215	ata Ile	738
														aaa Lys		786
														caa Gln		834

caa acc ttc ca Gln Thr Phe Gl 250					
gaa atg gtg aa Glu Met Val Ly 265				Cys Glu Ser	
gtg cag cgg ca Val Gln Arg Hi					
gcc ttg atg ga Ala Leu Met Gl 30	u Ser Leu				
gag aga acg ag Glu Arg Thr Ar 315			Ser Glu Gln		
ctc agt tta to Leu Ser Leu Tr 330					
ctg atg tat go Leu Met Tyr Al 345				Phe Pro Lys '	
gtc acc cac ag Val Thr His Se					
atg tac aga ct Met Tyr Arg Le 38	eu Tyr Gln				
gtt caa tcc gt Val Gln Ser Va 395			taactaggaa t	ggtcactgg	1313
gctgtttctt ca					1325
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<220> <221> misc_fe <223> At posi		t is a purine	.		
<400> 123					
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Glu Trp Thr Th		Thr Leu Leu 25	Pro Lys Tyr 1	Leu His Tyr 1 30	Asp

Pro Glu Thr Gly His Gln Leu Leu Cys Asp Lys Cys Ala Pro Gly Thr 35 40 45

Tyr Leu Lys Gln His Cys Thr Val Arg Arg Lys Thr Leu Cys Val Pro Cys Pro Asp His Ser Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys Val Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Ser Val Lys Gln Glu Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Glu Glu Gly Arg Tyr Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Ser Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Cys Pro Asp Gly Phe Phe Ser Gly Glu Thr Ser Ser Lys Ala Pro Cys 155 Ile Lys His Thr Asn Cys Ser Thr Phe Gly Leu Leu Ile Gln Lys Gly Asn Ala Thr His Asp Asn Cys Cys Ser Gly Asn Arg Glu Ala Thr Gln Lys Cys Gly Ile Asp Val Thr Leu Cys Glu Glu Ala Phe Phe Arg Phe Ala Val Pro Thr Lys Ile Ile Pro Asn Trp Leu Ser Val Leu Val Asp Ser Leu Pro Gly Thr Lys Val Asn Ala Glu Ser Val Glu Arg Ile Lys Arg Arg His Ser Ser Gln Glu Gln Thr Phe Gln Leu Leu Lys Leu Trp Lys His Gln Asn Arg Asp Gln Glu Met Val Lys Lys Ile Ile Gln Asp Ile Asp Leu Cys Glu Ser Ser Val Gln Arg His Leu Gly His Ser 280 Asn Leu Thr Thr Glu Gln Leu Leu Ala Leu Met Glu Ser Leu Pro Gly 295

Lys Lys Ile Ser Pro Glu Glu Ile Glu Arg Thr Arg Lys Thr Cys Lys 305 310 315 320	
Ser Ser Glu Gln Leu Leu Lys Leu Leu Ser Leu Trp Arg Ile Lys Asn 325 330 335	
Gly Asp Gln Asp Thr Leu Lys Gly Leu Met Tyr Ala Leu Lys His Leu 340 345 350	
Lys Thr Ser His Phe Pro Lys Thr Val Thr His Ser Leu Arg Lys Thr 355 360 365	
Met Arg Phe Leu His Ser Phe Thr Met Tyr Arg Leu Tyr Gln Lys Leu 370 380	
Phe Leu Glu Met Ile Gly Asn Gln Val Gln Ser Val Lys Ile Ser Cys 385 390 395 400	
Leu	
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cgyctccaag cccctgaggt ttccggggac caca atg aac aag ttg ctg tgc	115
Met Asn Lys Leu Cys Cys 1	-
gcg ctc gtg ttt ctg gac atc tcc att aag tgg acc acc cag gaa acg Ala Leu Val Phe Leu Asp Ile Ser Ile Lys Trp Thr Thr Gln Glu Thr 10 15 20	163
ttt cct cca aag tac ctt cat tat gac gaa gaa acc tct cat cag ctg Phe Pro Pro Lys Tyr Leu His Tyr Asp Glu Glu Thr Ser His Gln Leu 25 30 35	211
ttg tgt gac aaa tgt cct cct ggt acc tac cta aaa caa cac tgt aca Leu Cys Asp Lys Cys Pro Pro Gly Thr Tyr Leu Lys Gln His Cys Thr 40 45 50 55	259
gca aag tgg aag tcc gtg tgc gcc cct tgc cct gac cac tac tac aca Ala Lys Trp Lys Ser Val Cys Ala Pro Cys Pro Asp His Tyr Tyr Thr	307

	60	65	70
		t cta tac tgc agc ccc s Leu Tyr Cys Ser Pro 85	
		g tgc aat cgc acc cac u Cys Asn Arg Thr His 100	
		c ctt gag ata gag ttc r Leu Glu Ile Glu Phe 115	
		t gga gtg gtg caa gct e Gly Val Val Gln Ala 130	
		a tgt cca gat ggg ttc g Cys Pro Asp Gly Phe 145	
		t aga aaa cac aca aat s Arg Lys His Thr Asn 0 165	
		a gga aat gca aca cac s Gly Asn Ala Thr His 180	
		t caa aaa tgt gga ata r Gln Lys Cys Gly Ile 195	
		g ttt gct gtt cct aca g Phe Ala Val Pro Thr 210	
		a gac aat ttg cct ggc l Asp Asn Leu Pro Gly 225	
		a aaa cgg caa cac agc e Lys Arg Gln His Ser 0 245	
gaa cag act ttc Glu Gln Thr Phe 250	cag ctg ctg aag tta Gln Leu Leu Lys Leu 255	a tgg aaa cat caa aac u Trp Lys His Gln Asn 260	aaa gcc 883 Lys Ala
		a gat att gac ctc tgt n Asp Ile Asp Leu Cys 275	
		t aac ctc acc ttc gag a Asn Leu Thr Phe Glu 290	
		a aag aaa gtg gga gca y Lys Lys Val Gly Ala 305	
		a ccc agt gac cag atc s Pro Ser Asp Gln Ile	

	315			320					325			
ctg ctc agt Leu Leu Ser 330	Leu Trp	cga ata Arg Ile	a aaa E Lys 335	aat Asn	ggc Gly	gac Asp	caa Gln	gac Asp 340	acc Thr	ttg Leu	aag Lys	1123
ggc cta atg Gly Leu Met 345			His									1171
act gtc act Thr Val Thr 360												1219
aca atg tac Thr Met Tyr		Tyr Glr										1267
cag gtc caa Gln Val Gln	tca gta Ser Val 395	aaa ata Lys Ile	agc Ser	tgc Cys 400	tta Leu	taad	ctgga	aaa t	ggc	catt	ga	1317
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	_feature osition		ару	rimi	.dine	· .						
•			а ру	rimi	.dine	ė.						
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<223> At p <400> 125 Met Asn Lys	osition Leu Leu 5	63, Y is Cys Cys	: Ala	Leu	Val 10	Phe				15		
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Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg 135 Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys 150 155 160 Arg Lys His Thr Asn Cys Ser Val Phe Gly Leu Leu Thr Gln Lys Gly Asn Ala Thr His Asp Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr Gln Lys Cys Gly Ile Asp Val Thr Leu Cys Glu Glu Ala Phe Phe Arg Phe Ala Val Pro Thr Lys Phe Thr Pro Asn Trp Leu Ser Val Leu Val Asp Asn Leu Pro Gly Thr Lys Val Asn Ala Glu Ser Val Glu Arg Ile 230 Lys Arg Gln His Ser Ser Gln Glu Gln Thr Phe Gln Leu Leu Lys Leu Trp Lys His Gln Asn Lys Ala Gln Asp Ile Val Lys Lys Ile Ile Gln Asp Ile Asp Leu Cys Glu Asn Ser Val Gln Arg His Ile Gly His Ala Asn Leu Thr Phe Glu Gln Leu Arg Ser Leu Met Glu Ser Leu Pro Gly 290 295 300 Lys Lys Val Gly Ala Glu Asp Ile Glu Lys Thr Ile Lys Ala Cys Lys Pro Ser Asp Gln Ile Leu Lys Leu Leu Ser Leu Trp Arg Ile Lys Asn Gly Asp Gln Asp Thr Leu Lys Gly Leu Met His Ala Leu Lys His Ser Lys Thr Tyr His Phe Pro Lys Thr Val Thr Gln Ser Leu Lys Lys Thr

Ile Arg Phe Leu His Ser Phe Thr Met Tyr Lys Leu Tyr Gln Lys Leu

Phe Leu Glu Met Ile Gly Asn Gln Val Gln Ser Val Lys Ile Ser Cys

Leu

<210> 126

<211> 139

<212> PRT

<213> Homo sapiens

<400> 126

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Thr Lys Cys His Lys Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro

Gly Gln Asp Thr Asp Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr Ala

Ser Glu Asn His Leu Arg His Cys Leu Ser Cys Ser Lys Cys Arg Lys

Glu Met Gly Gln Val Glu Ile Ser Ser Cys Thr Val Asp Arg Asp Thr

Val Cys Gly Cys Arg Lys Asn Gln Tyr Arg His Tyr Trp Ser Glu Asn

Leu Phe Gln Cys Phe Asn Cys Ser Leu Cys Leu Asn Gly Thr Val His

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Phe Phe Leu Arg Glu Asn Glu Cys Val Ser Cys

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<211> 48

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<220>

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<211> 219

<212> PRT

<213> Rattus rattus

48

<400> 128

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Leu Glu Gly Leu His His Asp Gly Gln Phe Cys His Lys Pro Cys Pro 50 55 60

Pro Gly Glu Arg Lys Ala Arg Asp Cys Thr Val Asn Gly Asp Glu Pro 65 70 75 80

Asp Cys Val Pro Cys Gln Glu Gly Lys Glu Tyr Thr Asp Lys Ala His
85 90 95

Phe Ser Ser Lys Cys Arg Arg Cys Arg Leu Cys Asp Glu Gly His Gly 100 105 110

Leu Glu Val Glu Ile Asn Cys Thr Arg Thr Gln Asn Thr Lys Cys Arg 115 120 125

Cys Lys Pro Asn Phe Phe Cys Asn Ser Thr Val Cys Glu His Cys Asp 130 135 140

Pro Cys Thr Lys Cys Glu His Gly Ile Ile Lys Glu Cys Thr Leu Thr 145 150 155 160

Ser Asn Thr Lys Cys Lys Glu Glu Gly Ser Arg Ser Asn Leu Gly Trp 165 170 175

Leu Cys Leu Leu Leu Pro Ile Pro Leu Ile Val Trp Val Lys Arg 180 185 190

Lys Glu Val Gln Lys Thr Cys Arg Lys His Arg Lys Glu Asn Gln Gly 195 200 205

Ser His Glu Ser Pro Thr Leu Asn Pro Glu Thr 210 215

<210> 129

<211> 281 <212> PRT

<213> Rattus rattus

<400> 129

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His Leu Gly Asp Arg Glu Lys Arg Asp Ser Val Cys Pro Gln Gly Lys 35 40 45

Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr Lys Cys His Lys 50 55 60

Gly Thr Tyr Leu Thr Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr

70 75 65 80 Asp Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu Arg His Cys Leu Ser Cys Ser Lys Cys Arg Lys Glu Met Gly Gln Val Glu Ile Ser Ser Cys Thr Val Asp Arg Asp Thr Val Cys Gly Cys Arg Lys Asn Gln Tyr Arg His Tyr Trp Ser Glu Asn Leu Phe Gln Cys Phe Asn Cys Ser Leu Cys Leu Asn Gly Thr Val His Leu Ser Cys Gln 155 Glu Lys Gln Asn Thr Val Cys Thr Cys His Ala Gly Phe Phe Leu Arg Glu Asn Glu Cys Val Ser Cys Ser Asn Cys Lys Lys Ser Leu Glu Cys Thr Lys Leu Cys Leu Pro Gln Ile Glu Asn Val Lys Gly Thr Glu Asp 200 Ser Gly Thr Thr Val Leu Leu Pro Leu Val Ile Phe Phe Gly Leu Cys Leu Leu Ser Leu Leu Phe Ile Gly Leu Met Thr Arg Thr Gln Arg Trp Lys Ser Lys Leu Tyr Ser Ile Val Cys Gly Lys Ser Thr Pro Glu Lys 245 250 255 Glu Gly Glu Leu Glu Gly Thr Thr Thr Lys Pro Leu Ala Pro Asn Pro 265 Ser Phe Ser Pro Thr Pro Gly Phe Thr 275 <210> 130 <211> 207 <212> PRT <213> Rattus rattus <400> Met Leu Arg Leu Ile Ala Leu Leu Val Cys Val Val Tyr Val Tyr Gly $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ Asp Asp Val Pro Tyr Ser Ser Asn Gln Gly Lys Cys Gly Gly His Asp 20 25 30Tyr Glu Lys Asp Gly Leu Cys Cys Ala Ser Cys His Pro Gly Phe Tyr Ala Ser Arg Leu Cys Gly Pro Gly Ser Asn Thr Val Cys Ser Pro Cys 50 55 60 Glu Asp Gly Thr Phe Thr Ala Ser Thr Asn His Ala Pro Ala Cys Val Ser Cys Arg Gly Pro Cys Thr Gly His Leu Ser Glu Ser Gln Pro Cys

85 90 95 Asp Arg Thr His Asp Arg Val Cys Asn Cys Ser Thr Gly Asn Tyr Cys Leu Leu Lys Gly Gln Asn Gly Cys Arg Ile Cys Ala Pro Gln Thr Lys Cys Pro Ala Gly Tyr Gly Val Ser Gly His Thr Arg Ala Gly Asp Thr 135 Leu Cys Glu Lys Cys Pro Pro His Thr Tyr Ser Asp Ser Leu Ser Pro Thr Glu Arg Cys Gly Thr Ser Phe Asn Tyr Ile Ser Val Gly Phe Asn Leu Tyr Pro Val Asn Glu Thr Ser Cys Thr Thr Thr Ala Gly His Asn Glu Val Ile Lys Thr Lys Glu Phe Thr Val Thr Leu Asn Tyr Thr 200 <210> 131 <211> 227 <212> PRT <213> Rattus rattus <400> Met Ala Pro Val Ala Val Trp Ala Ala Leu Ala Val Gly Leu Glu Leu Trp Ala Ala Ala His Ala Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Thr Thr Asp Gln Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp 65 70 75 80 Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu 115 120 125Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr

Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro Gly

180 185 190

Asn Ala Ser Arg Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser 195 200 205

Met Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser 210 215 220

Gln His Thr 225

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<211> 197

<212> PRT

<213> Rattus rattus

<400> 132

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His Asp Gly Gln Cys Cys Asp Leu Cys Gln Pro Gly Ser Arg Leu Thr 35 40 45

Ser His Cys Thr Ala Leu Glu Lys Thr Gln Cys His Pro Cys Asp Ser 50 55 60

Gly Glu Phe Ser Ala Gln Trp Asn Arg Glu Ile Arg Cys His Gln His 65 70 75 80

Arg His Cys Glu Pro Asn Gln Gly Leu Arg Val Lys Lys Glu Gly Thr 85 90 95

Ala Glu Ser Asp Thr Val Cys Thr Cys Lys Glu Gly Gln His Cys Thr 100 105 110

Ser Lys Asp Cys Glu Ala Cys Ala Gln His Thr Pro Cys Ile Pro Gly
115 120 125

Phe Gly Val Met Glu Met Ala Thr Glu Thr Thr Asp Thr Val Cys His 130 140

Pro Cys Pro Val Gly Phe Phe Ser Asn Gln Ser Ser Leu Phe Glu Lys 145 150 155 160

Cys Tyr Pro Trp Thr Ser Cys Glu Asp Lys Asn Leu Glu Val Leu Gln
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Arg Ala Leu Leu Val 195

<210> 133

<211> 208

<212> PRT

<213> Rattus rattus

<400> 133

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Ala Pro Cys Val Glu Ala Asp Asp Ala Val Cys Arg Cys Ala Tyr Gly Tyr Tyr Gln Asp Glu Thr Thr Gly Arg Cys Glu Ala Cys Arg Val Cys Glu Ala Gly Ser Gly Leu Val Phe Ser Cys Gln Asp Lys Gln Asn Thr Val Cys Glu Glu Cys Pro Asp Gly Thr Tyr Ser Asp Glu Ala Asn His Val Asp Pro Cys Leu Pro Cys Thr Val Cys Glu Asp Thr Glu Arg Gln Leu Arg Glu Cys Thr Arg Trp Ala Asp Ala Glu Cys Glu Glu Ile Pro Gly Arg Trp Ile Thr Arg Ser Thr Pro Pro Glu Gly Ser Asp Ser Thr 200 Ala Pro Ser Thr Gln Glu Pro Glu Ala Pro Pro Glu Gln Asp Leu Ile <210> 135 <211> 205 <212> PRT <213> Rattus rattus <400> 135 Met Tyr Val Trp Val Gln Gln Pro Thr Ala Phe Leu Leu Gly Leu Ser Leu Gly Val Thr Val Lys Leu Asn Cys Val Lys Asp Thr Tyr Pro Ser Gly His Lys Cys Cys Arg Glu Cys Gln Pro Gly His Gly Met Val Ser Arg Cys Asp His Thr Arg Asp Thr Val Cys His Pro Cys Glu Pro Gly Phe Tyr Asn Glu Ala Val Asn Tyr Asp Thr Cys Lys Gln Cys Thr Gln Cys Asn His Arg Ser Gly Ser Glu Leu Lys Gln Asn Cys Thr Pro Thr Glu Asp Thr Val Cys Gln Cys Arg Pro Gly Thr Gln Pro Arg Gln Asp Ser Ser His Lys Leu Gly Val Asp Cys Val Pro Cys Pro Pro Gly His Phe Ser Pro Gly Ser Asn Gln Ala Cys Lys Pro Trp Thr Asn Cys

Thr Leu Ser Gly Lys Gln Ile Arg His Pro Ala Ser Asn Ser Leu Asp

Thr Val Cys Glu Asp Arg Ser Leu Leu Ala Thr Leu Leu Trp Glu Thr

165

Gln Arg Thr Thr Phe Arg Pro Thr Thr Val Pro Ser Thr Thr Val Trp Pro Arg Thr Ser Gln Leu Pro Ser Thr Pro Thr Leu Val 200 <210> 136 <211> 191 <212> PRT <213> Rattus rattus <400> 136 Met Gly Asn Asn Cys Tyr Asn Val Val Ile Val Leu Leu Val Gly Cys Glu Lys Val Gly Ala Val Gln Asn Ser Cys Asp Asn Cys Gln Pro Gly Thr Phe Cys Arg Lys Tyr Asn Pro Val Cys Lys Ser Cys Pro 35 40 45Pro Ser Thr Phe Ser Ser Ile Gly Gly Gln Pro Asn Cys Asn Ile Cys Arg Val Cys Ala Gly Tyr Phe Arg Phe Lys Lys Phe Cys Ser Ser Thr 65 70 75 80 His Asn Ala Glu Cys Glu Cys Ile Glu Gly Phe His Cys Leu Gly Pro 85 90 95 Gln Cys Thr Arg Cys Glu Lys Asp Cys Arg Pro Gly Gln Glu Leu Thr Lys Gln Gly Cys Lys Thr Cys Ser Leu Gly Thr Phe Asn Asp Gln Asn Gly Thr Gly Val Cys Arg Pro Trp Thr Asn Cys Ser Leu Asp Gly Arg 135 Ser Val Leu Lys Thr Gly Thr Thr Glu Lys Asp Val Val Cys Gly Pro Pro Val Val Ser Phe Ser Pro Ser Thr Thr Ile Ser Val Thr Pro Glu Gly Gly Pro Gly Gly His Ser Leu Gln Val Leu Thr Leu Phe Leu <210> 137 <211> 54 <212> DNA <213> Artificial Sequence <220> <221> misc_feature <223> Oligonucleotide capable of hybridizing to human sequence. tatggatgaa gaaacttctc atcagctgct gtgtgataaa tgtccgccgg gtac

54

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<210> 139

<211> 380

<212> PRT

<213> Homo sapiens

<400> 139

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Pro Ly	s Thr	Val 340	Thr	GIn	Ser	Leu	Lys 345	Lys	Thr	Ile	Arg	Phe 350	Leu	His	
Ser Ph	e Thr 355	Met	Tyr	Lys	Leu	Туг 360	Gln	Lys	Leu	Phe	Leu 365	Glu	Met	Ile	
Gly As 37		Val	Gln	Ser	Val 375	Lys	Ile	Ser	Cys	Leu 380					
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      PCR primer for deletion mutant.
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0.1.0	4.50	
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<223>		

168 <400 >

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